Citation:

Teede HJ, Dalais FS, Kotsopoulos D, Liang Y, Davis S, McGrath BP. Dietary soy has both beneficial and potentially adverse cardiovascular effects: A placebo-controlled study in men and postmenopausal women. *The Journal of Clinical Endocrinology and Metabolism,* 2001; 86: 3,053-3,060.

PubMed ID: 11443167

Study Design:

RCT

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine the effect of dietary soy supplementation on lipid parameters, blood pressure, arterial compliance and endothelial function.

Inclusion Criteria:

- No consumption of antibiotics, soy products or supplements for three months for men and women
- For women, 12 months of amenorrhea and FSH greater than 20IU per L and 12 months without estrogen therapy.

Exclusion Criteria:

- Moderate to severe menopausal symptoms
- Smoking in the last 10 years
- Alcohol consumption above 30g per day
- Hypertension
- Abnormal uterine bleeding
- Cervical cytology or mammogram and coexistent major illness.

Description of Study Protocol:

Recruitment

Community advertisement.

Design

- A double-blind, randomized, placebo-controlled study of the addtition of soy to the diets of

normotensive men and post-menopausal women
- 105 participants (50 women and 55 men) were randomized to treatment with soy
- 108 (55 women and 53 men) were randomized to casein placebo
- Participants consumed the supplements twice daily (in beverage form) in addition to their usual diet with no other modifications.

Blinding Used

Supplements were identical in appearance.

Intervention

Forty grams soy-protein isolate with 118mg isoflavones or casein placebo for three months.

Statistical Analysis

- Change in variables from baseline to endpoint were analyzed with MANOVA with backward elimination of variables to establish the final model
- The Ryan-Holm step-down Bonferroni procedure was used to control for the risk of type I error with multiple hypothesis testing.

Data Collection Summary:

Timing of Measurements

Baseline and three months.

Dependent Variables

- Mean, systolic and diastolic BP
- Total, LDL, HDL cholesterol and LDL-HDL ratio
- Triglycerides
- Lipoprotein (a)
- *Vascular parameters:* Total systemic arterial compliance (SAC), pulse wave velocity (PWV) and brachial artery FMD.

Independent Variables

- 40g soy-protein isolate with 118mg isoflavones or casein placebo for three months
- Dietary adherence assessed by measurement of spot urine phytoestrogen concentrations at baseline and at the end of three months.

Description of Actual Data Sample:

- *Initial N:* 213, 108 men, 105 postmenopausal women
- *Attrition (final N):* 179, 83 women, 96 men. 84% completion
- Age
    - *Soy group, mean:* 61±1 years
    - *Placebo group, mean:* 60±1 years
- *Ethnicity:* Not specified.
- *Anthropometrics:* Baseline parameters were similar between groups.
- *Location:* Australia.

Summary of Results:

Variables	Soy Supplement			Casein Placebo		
	Baseline	*Three Months*	*Mean Change, Baseline to Three Months*	*Baseline*	*Three months*	*Mean Change, Baseline to Three Months*
Mean ± BP	93±1	87±1	-5.5±1.0[a]	91±1	89±1	- 1.3±0.9
Systolic BP	130±2	123±2	-7.5±1.2[b]	128±2	125±2	-3.6±1.1
Diastolic BP	76±1	72±1	-4.3±0.8[b]	76±2	73±1	-1.9±0.7
Total cholesterol	5.9±0.1	5.3±0.1	-0.05±0.09	5.9±0.1	5.5±0.1	-0.4±0.09
LDL Cholesterol	3.9±0.1	3.5±0.1	-0.42±0.07	3.8±0.1	3.6±0.1	-0.28±0.07
HDL Cholesterol	1.44±0.01	1.40±0.04	-0.04±0.03	1.51±0.1	1.40±0.05	-0.11±0.04
LDL/HDL Cholesterol	3.1±0.2	2.7±0.1	-0.33±0.09	2.8±0.2	2.8±0.1	-0.04±0.08
Triglycerides	1.2±0.1	1.0±0.07	-0.19±0.05	1.2±0.1	1.2±0.07	0.01±0.05
Lipoprotein (a)	286 (207-365)	328 (235-421)	42 (17-67)	341 (251-433)	346 (252-440)	4 (-22-30)

Other Findings

- Soy supplementation had no significant effect on arterial compliance by MANOVA
- On univariate ANOVA, only PW improved significantly.

Author Conclusion:

- In normotensive men and post-menopausal women, soy improved BP and lipids, but overall, did not improve vascular function
- Further research in hypertensive and hyperlipidemic populations is needed.

Reviewer Comments:

Dietary adherence assessed by measurement of spot urine phytoestrogen concentrations at baseline and at the end of three months.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes

3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A

3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	No
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A

6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	No
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	No
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes

10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes